PHILIP MORRIS
U.S.A.
Research Center, Richmond, Virginia 23261-6583

RICHARD A. CARCHMAN, PhD
Vice President
Scientific Affairs

P.O. Box 26583
(804)274-5794
Fax: (804)274-2891

March 20, 1998

VIA FEDERAL EXPRESS

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
79 Alexander Drive
Building 4401, Room 3127
Research Triangle Park, NC 27709

VIA EXPRESS MAIL

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14
P.O. Box 12233
Research Triangle Park, NC 27709

Re: Comments on NTP's proposal for listing environmental tobacco smoke (ETS) in the Report on Carcinogens, Ninth Edition

Dear Dr. Jameson:

Philip Morris U.S.A. welcomes this opportunity to comment on the National Toxicology Program's (NTP's) intent to review environmental tobacco smoke (ETS) for possible listing in the *Report on Carcinogens, Ninth Edition*, as noticed in 63 *Fed. Reg.* 5565, February 3, 1998. We understand that these comments, postmarked March 20, 1998, 45 days after the date of publication of the notice, will be accepted as timely and provided to NTP's reviewers. We are sending one bound copy by Federal Express and one unbound copy by Express Mail for your convenience in photocopying.

Philip Morris believes that, at this time, a scientific classification of ETS as a "known human carcinogen" would be premature because existing scientific support with respect to ETS is neither persuasive nor conclusive, and because a number of important critical scientific questions remain unanswered.

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Source: https://www.industrydocuments.ucsf.edu/docs/kknj0001

We therefore submit, for your reference, a listing of currently available studies and reviews from the scientific literature that do not support the classification of ETS as a known human carcinogen. [Attached to this correspondence, Appendix 1]

Philip Morris USA also is committed to addressing remaining questions regarding ETS through support of scientific research. We have, for example, initiated an on-going research program which is evaluating the biological activity of an ETS surrogate (room-aged sidestream smoke (RASS)). Our submission contains a publication on the methodology for analyzing RASS, as well as a publication of a subchronic study of inhalation exposure of rats to RASS. [See Appendix 2] The biological effects observed to date are indicative of mild irritation that is both reversible and non-progressive. We anticipate completion of the study within two years; as additional data are published, they will be forwarded to you for your review.

We have also supported research and analysis of the smoke components, tobacco specific nitrosamines (TSNAs), that have been purported to be causally associated with lung cancer. A comparative analysis of TSNA metabolism in lung and liver from the A/J mouse, Fischer 344 rat and human strongly indicates that activation predominates in the mouse and rat, but that in human tissues, a detoxification process predominates. This suggests that though TSNAs may be animal carcinogens (consistent with the metabolic profile reported here), in humans, the metabolic profile of TSNAs **is not** consistent with carcinogenic activity. [See Appendix 3]

In addition to the foregoing, Philip Morris U.S.A. submits the following materials for consideration in NTP's review of ETS for listing in the *Ninth Report on Carcinogens*. Included are the following items:

- A discussion of the recent report from the International Agency for Research on Cancer (IARC) on its multi-center epidemiologic study of ETS exposure and lung cancer risk in Europe (IARC Biennial Report 1996/1997). The IARC study, the largest, and according to IARC, the "most comprehensive" epidemiological study specifically designed to assess the potential lung cancer risk of spousal, workplace and childhood ETS exposure, reported no statistically significant risk estimates for spousal, workplace, spousal plus workplace or childhood exposures. [See Appendix 4]

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- An additional analysis of the United States Environmental Protection Agency's (U.S. EPA) 1992 Risk Assessment on ETS, which addresses, using Monte Carlo simulations, the uncertainty associated with two critical factors that influence the attributable deaths estimated by EPA.[1] Our analysis indicates that proper consideration of just these two factors reduces the EPA's attributable risk number by two-thirds. Further consideration of factors such as diet, socio-economic status, family history of lung disease, etc., as well as data from epidemiologic and exposure studies in the workplace, social settings, etc., would be expected to further reduce this estimate. [See Appendix 5]

- Our analysis of methodologies utilizing cotinine as a measure of either smoking status or ETS exposure. The technological measurement short-comings and the metabolic complexities of these issues lead us to describe what we believe to be a more systematic and rigorous approach to this question. Given the current situation, we believe that the use of single point measurements using cotinine alone cannot be used as a quantitative measure of ETS exposure. [See Appendix 6]

- An analysis of the smoke component, benzo(a)pyrene (B(a)P), that has been purported to be causally associated with lung cancer. This analysis suggests the following: (i) that the levels of B(a)P that would be expected in environments where ETS is present are within the background levels found in urban air and (ii) that sources other than ETS account for more than 90 percent (>90%) of the total body burden of B(a)P. [See Appendix 7]

- Philip Morris' 1997 submission to the California Environmental Protection Agency (Cal/EPA) addressing the alleged association between reported exposure to ETS and human cancer. [See Appendix 8]

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1. For the purpose of demonstrating the fragility of the U.S. EPA's attributable death calculations in its Risk Assessment on ETS (1992), we utilized EPA's relative risk point estimate. It is important to note that we do not believe that this point estimate is scientifically justified. In fact, the data indicate that one cannot distinguish the association between reported exposure to ETS and lung cancer described by the EPA from no association.

Source: https://www.industrydocuments.ucsf.edu/docs/kknj0001

We believe that the underlying science, including ETS exposure as determined by personal monitoring, distributional analysis of exposure information, human epidemiological and biomonitoring data and animal studies, support the scientific position that environmental tobacco smoke cannot be classified as a known human carcinogen.

Sincerely,

Richard A. Carchman, Ph.D.

RAC/jk

Enclosure(s)

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